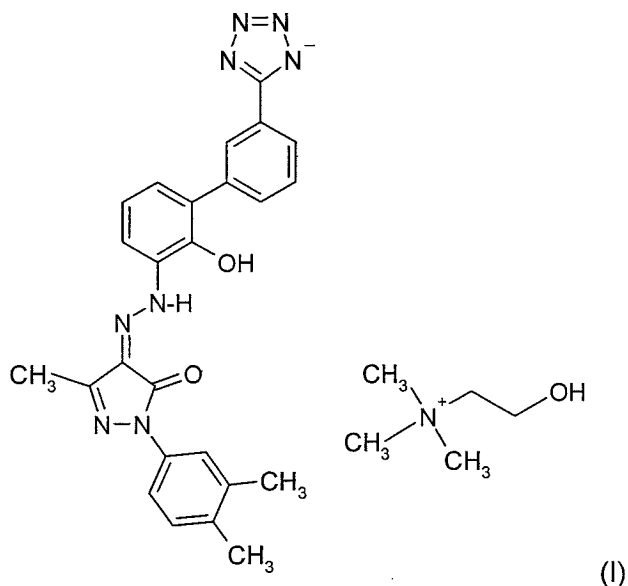


Amendments to the Specification:

Amended pages 1 and 12 are indicated below. Figure 1 on a separate paper is attached. Please insert the attached Figure 1 after the claims.

2-(3,4-DIMETHYLPHENYL)-4-[[2-HYDROXY-3'-(1H-TETRAZOL-5-YL)BIPHENYL-3-YL]-HYDRAZONO]-5-METHYL-2,4-DIHYDROPYRAZOL-3-ONE CHOLINE

This invention relates to an improved thrombopoietin (hereinafter TPO) mimetic, the choline salt of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono]-5-methyl-2,4-dihydropyrazol-3-one. The compound is represented by Structure I:



The compound of this invention is useful as an agonist of the TPO receptor, particularly in enhancing platelet production.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure - 1 Figure 1 depicts an X-ray powder diffraction pattern of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono]-5-methyl-2,4-dihydropyrazol-3-one choline.

Detailed Description of the Invention

2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono]-5-methyl-2,4-dihydropyrazol-3-one is a compound which is disclosed and claimed, along with pharmaceutically acceptable salts, hydrates, solvates and esters thereof, as being useful as an agonist of the TPO receptor, particularly in enhancing platelet production and particularly in the treatment of thrombocytopenia, in International Application No. PCT/US01/16863, having an International filing date of May 24, 2001; International Publication Number WO 01/89457 and an International Publication date of November 29, 2001 (compound of Example 12), the entire disclosure of which is hereby

2-(3,4-Dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono]-5-methyl-2,4-dihydropyrazol-3-one, 1.1 g of crude orange solid, in 7 mL of ethyl acetate and 12 mL of ethanol (190 proof) was stirred at approximately 40°C. To this suspension 2.5 ml of choline hydroxide (1N) solution in methanol was added resulting in a dark orange brown solution. Water (1 ml) was added to the dark solution and the mixture stirred at approx. 35 °C for approx. 3 hours. During this time, precipitation was seen in the solution. The suspension was stirred for another 72 hours at approx. 20 °C, and then the solid was isolated by filtration and dried at approx. 40 °C over 12 hours to yield 1.2 gram (87% yield) of the title compound as a crystalline solid with a light orange color.

The solid was proved to be crystalline by X-ray powder diffraction taken on a Philips X'Pert Pro diffractometer. The sample was scanned with the following parameters: scan range: 2-35 degrees two-theta; generator power: 40kV, 40mA; radiation source: Cu K α ; scan type: continuous; step time: 10.16 seconds; step size: 0.0167 degrees two-theta per step; sample rotation: 25 rpm. Following are the is an X-ray powder pattern and peak list. An X-ray powder pattern is depicted in Figure 1.

